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(71) Applicant: **MICROBYX CORPORATION**
49 Locust Avenue
New Canaan, Connecticut 06840(US)

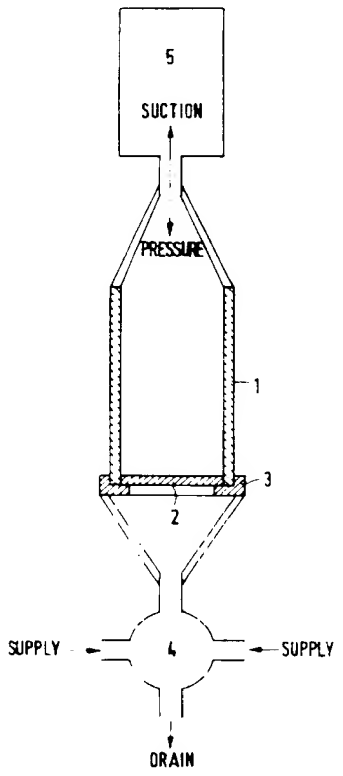
(72) Inventor: **Andresen, John A.**
49 Locust Avenue
New Canaan, Connecticut 06840(US)

(74) Representative: **Kinzebach, Werner, Dr. et al**
Patentanwälte Reitstötter, Kinzebach und Partner Sternwartstrasse 4 Postfach 86 06 49
W-8000 München 86(DE)

(54) Automated pap test method and device.

(57) Blood collected by tampons and the like is subjected to the same type of analysis as Pap Smear analysis in a rapid manner which can be automated. The collected blood, particularly menstrual blood, is filtered through a filter with openings sufficiently small to permit cells not of clinical interest to pass through the filter while retaining the cells of clinical interest. The cells of clinical interest are subjected to washings and back washings and then subjected sequentially to the generally 18 Pap solutions, at the end of which the cells are placed on a slide and read by a cytologist or by computer.

FIG.1



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BACKGROUND OF THE INVENTION

The current Pap Test requires the gynecologist to take a specimen by scraping or smear from the cervix, using a spatula or swab and rubbing the material onto a slide. The slide is sprayed with a fixative to preserve the specimen and is then transported to the lab. The specimen is then placed into a slide holder (along with many other slides - as many as twenty or more - and from many other patients, and dipped either by hand or by automatic dipping machine into the various Pap Test solutions (approximately 18) each of which is contained in its own vessel. The vessels used are small, usually glass, usually rectangular tubs.

During this process, cells fall or float off each patient's slide and settle to the bottom of the vessel and/or stick to other patient's slides. After several sets of slides have been dipped into a vessel, a layer of specimen material, including cells, may be found at the bottom of the vessel. Moreover, with each dipping, the composition of the solution in each vessel is changed by carry over of solution from the preceding vessel and by material floating or falling off the slides.

This overall procedure is time consuming and can be wrought with many inaccuracies resulting from the above steps and/or cause variable output in terms of stained slide with each set of slides also differing from each other in terms of staining.

Patent No. RE 29,061 describes a method for collecting and analyzing blood by introducing into a cavity of the person, for example the vagina in the case of a woman, of a device which has an interior capable of receiving and holding blood which is present in the cavity. For example, the device may be a tampon inserted by a woman into the vagina for collecting the blood during menstrual flow. The blood thus collected can be subjected to analysis, for example Pap Test analysis.

The method and device for collecting blood as set forth in Patent No. RE 29,061 provides greater accuracy for analysis than does the ordinary Pap smear or scrapping test. However, the very simplicity of the method and device of Patent No. RE 29,061 leads to the problem of a need for more rapid and possibly automated analysis because the method and device do not require the gynecologist, and the laboratories could be flooded with collections requiring analysis. Still further greater accuracy of analysis is required because of the large number of collections obtained for analysis.

SUMMARY OF THE INVENTION

It is accordingly a primary object of the present invention to provide a method for rapid and accurate analysis of blood, particularly blood collected by tampons and the like during menstrual flow.

It is another object of the present invention to provide a device for receiving a tampon or the like containing menstrual blood flow for rapid and accurate treatment in a device in which all of the stages of a Pap Test can be carried out up to the point of analysis of cells deposited on a glass slide.

It is yet another object of the present invention to provide a device for sequential contact with Pap solutions for rapid and accurate analysis of cells.

Other objects and advantages of the present invention will be apparent from a reading of the specification and of the appended claims.

With the above and other objects in view, the present invention mainly comprises a method of analysis of menstrual blood flow wherein menstrual blood collected by a tampon or the like, which blood would include cells of clinical interest, is deposited in a container provided with a filter having a pore size such that all cells of clinical interest in the blood specimen cannot pass through the filter and cells which are not of clinical interest for example red and white blood cells are small enough to pass through the filter, subjecting the menstrual blood in the container to washings and back washings, for example with saline solution or balanced salt solution, e.g. Ringer's solutions, and further subjecting the suspended cells to the approximately 18 Pap solutions after which the cells remaining in the container are deposited on a glass slide and analyzed by the cytologist. The analysis can be by way of standard slide examination or utilizing computers.

The filter used in the container of the invention is preferably a 12-micron pore size filter. Cells of clinical interest are substantially larger than 25 microns and cannot go through the pores of the filter. On the other hand, the cells that are not of clinical interest, for example red and white blood cells which have a size of about 7 microns, are small enough to go through the filter pores and are removed from the specimen along with the blood plasma. This is accomplished by repeated washings and back washings.

Although 12-micron pore filters are preferred, it is possible to use filters in the range of 5-12 microns. When filters of 5-8 micron size are used, 7-micron red blood cells and 12-micron white blood cells can still be forced through the filters by pressure.

This same container, which now contains only the cells of clinical interest is then subjected to the approximately 18 Pap solutions which are generally sequentially introduced into the container in an amount to fill the same, then removed until the final cells are stained in accordance with the Pap process, after which the cells are evenly deposited on a glass slide with or without a filter.

By proceeding in accordance with this method, cells of clinical interest in any specimen are entrapped because these cells cannot enter or leave, so that there is no loss or gain of cells of clinical interest. All other cells and fluids are washed out so that at the end only a clean suspension of cells of clinical interest is obtained which cells are processed through the Pap solutions, in suspension, reducing overall time, increasing quality and resulting in uniformity of analysis. The overall process results in a saving in labor, materials, time, and of course therefore in costs.

The increased quality and greater uniformity of test results by proceeding in accordance with the method of the present invention are achieved as a result of many advantages derived from proceeding in accordance with the method of the invention.

Thus, for example, the washings and Pap solutions used according to the present invention cannot result in either the loss of cells of clinical interest or the contamination of the cells in the container by another patient's cells. Thus, cells of clinical interest cannot get in or out of the container and other cells cannot get into the container.

The time required for cell contact of the cells with the various Pap solutions is substantially reduced as compared to proceeding in accordance with the normal Pap procedure because the cells are in suspension rather than being flat on a slide. Furthermore, the amount of solution is greatly reduced since only a few ml of solution are required to fill the container.

In accordance with the method of the invention, fresh solution is used each time with the solution sent to drain after each use, so that each specimen is stained in the same consistent way. Furthermore, at the end of the Pap process, the cells are evenly deposited on a glass slide, with or without the filter.

The general procedure according to the present invention is as follows:

The tampon used during menstrual flow, after removal from the woman, is placed in a vial containing fixative solution. The vial is sealed and transported to the laboratory. At the laboratory the vial is shaken, inverted, swirled, or mildly sonicated to move cells from the tampon into the fixative solution and to create a cell suspension in the fixative solution. The tampon is removed and discarded.

The cell suspension is poured into a disposable plastic syringe with a filter holder containing a 5-12 micron pore filter, preferably a 12 micron pore filter. The cells are washed and back washed by passing solutions through the filter until the blood and mucous have been removed. After the last washing, the cells are subjected to the standard Pap solutions, left on the filter and the filter is clipped to a glass slide and analyzed by the cytologist.

For large scale analyses the procedure is as follows:

Each of the tampons is inserted into a separate vial containing fixative solution and the vials are placed into machines which mildly sonicate the same to move cells from the the tampon into the fixative solution and to create a cell suspension in the fixative solution. The cell suspension is aspirated by the machine into a modified disposable plastic syringe with a filter holder containing a 12 micron filter. The vial and tampon are removed and discarded by the machine.

The machine automatically works the modified disposable plastic syringe to wash and backwash the cells until the blood and mucous have been removed. The machine then automatically moves the modified disposable plastic syringe to expose the cells sequentially to each and all of the solutions used in the standard Pap method. This can be done either by moving the syringe to each solution in turn, or by moving each solution in turn to the syringe. In either case, a solution is used once and then sent to drain.

After the standard Pap method treatment has been completed the machine can either place the filter on a glass slide or centrifuge the cells onto a glass slide. In either case, the cells are ready to be read by the cytologist without ever having been touched by any hands, completely automatically.

In accordance with another embodiment the cell suspension after the standard Pap Test has been completed is introduced into a currently commercially available cell counter sorter (laser microscope) which reads the cells, separates abnormal and suspicious cells, and puts them on a slide for the cytologist. The machine also prints out a report. This possibility does not exist in the case of the ordinary Pap Smear test because it is not possible by such [illegible] to obtain a sufficient number of cells in suspension. This is only possible with the collection [illegible] blood by a tampon or the like and by [illegible] as set forth herein.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention is illustrated by way of example in the accompanying drawings which form part of this invention and in which:

Fig. 1 is a schematic illustration of a device according to the invention in which a vial or cylinder is provided with a single filter;

Fig. 2 is a schematic illustration of another embodiment of the invention in which a vial or cylinder is provided with two filters;

Fig. 3 is a schematic illustration of a device for sonicating specimens in the original collection container; and

Fig. 4 is a schematic illustration of a device wherein liquids used in processing the cells are controlled by valves.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Fig. 1 illustrates a cylinder 1 provided with a filter 2 at one end thereof so that treating liquid may be introduced through the filter and discharged through the same filter. The filter 2 is held by filter holder ring 3. The treating liquid is alternately driven in and out of the cylinder 1 through the filter 2 by means of pressure-vacuum pump 5 with control by means of solenoid valve 4.

In the embodiment of Fig. 2, the cylinder 1' is provided with two filters, 2', one at each end of the cylinder, each held by a filter holder ring 3'. Pump 5' provides suction for drawing the treating liquid in the direction through the filters 2' with valves 4' opening and closing as needed.

As illustrated in Fig. 3, a collection container 6 containing the specimen 8 is sonicated by means of sonicator 7 to move the cells into suspension in the treating liquid. By means of aspirator 9 and pump 10 the liquid 8 containing the suspended cells is aspirated, with the aid of pump 10 into cylinder 11 provided with a filter 12 which is held by filter holder ring 13. The thus aspirated suspended specimen is then subjected to treatment with the Pap solutions.

As illustrated in the embodiment of Fig. 4, reservoirs 14, 14a, 14b, etc., each containing a different Pap solution used in the Pap method are alternately supplied by means of control valves 15 and 16 to the cylinder for treatment of the cells therein. Each liquid, alcohol, stain, etc., is passed into the cylinder and then withdrawn from the cylinder. Supply 17 illustrates the possibility of various treating solutions entering the system from a different entrance.

In carrying out the method of the present invention, the tampon after removal from the woman is placed into a vial containing a fixative solution. The fixative is used in cytology to maintain the existing form and structure of the cells, particularly the nuclear detail. The fixative solution may be, for example, 10% neutral buffered formalin or dilute methyl or ethyl alcohol, or it may be a mixture of alcohol and wax, which forms a thin, protective coating over the cells and preserves the same until they are processed in the cytology laboratory.

At the laboratory, the vial containing the tampon in the fixitive solution is shaken or sonicated to create a cell suspension in the solution. The tampon is removed and discarded.

The cell suspension is introduced into the disposable plastic syringe provided with a filter holder containing a 5-12 micron filter, preferably 12-micron filter. The cells are washed and backwashed until blood and mucous have been removed leaving only the cells of clinical interest on the filter. These cells are then subjected to the Pap stain solutions for visualization of cellular changes. The stain is basically composed of a blue nucleus stain and orange, red, and green cytoplasmic counter stains. The nuclear stain demonstrates the chromatin patterns associated with normal and abnormal cells, while the cytoplasmic stains help to indicate cell origin. The cells are generally subjected to about 18 or more different staining solutions, after which the filter is placed upon a glass slide or the cells are centrifuged onto the glass slide, after which the cytologist can read the slide.

While normal pap testing provides only about ninety percent accuracy, the above method provides accuracy approaching one hundred percent.

Claims

1. Method of Pap analysis which comprises introducing a collected menstrual blood specimen into a container provided with a filter having a pore size sufficiently large to permit cells which are not of clinical interest to pass through the same while being sufficiently small to prevent cells of clinical interest from passing through the same, subjecting the thus collected specimen to washings through the filter to remove blood, mucous and other cells not of clinical interest from the container while retaining cells of clinical interest on the filter, subjecting the cells collected on the filter to Pap solutions and subjecting the thus Pap solution treated cells to analysis by a cytologist on a slide or by computer analysis.

2. Method according to claim 1, wherein said filter has an approximately 5-12 micron pore size.

3. Method according to claim 2, wherein said filter has an approximately 12-micron pore size.

4. Method according to claims 1-3,wherein collected menstrual blood is contacted with a fixative solution, the fixative solution and menstrual blood are shaken or sonicated to suspend cells from the blood specimen in the fixative solution, the thus obtained fixative solution containing suspended cells is introduced into the container provided with the filter after which the washings and Pap solution treatment steps proceed.

5. Method according to claim 4, wherein the menstrual blood is collected by means of a tampon which is introduced into the fixative solution and after shaking or sonication to suspend the cells in the fixative solution the tampon is removed and discarded.

6. Method according to claims 1-5, wherein the container is provided with a single filter and the specimen is washed and back washed through the same filter.

7. Method according to claims 1-5, wherein the container is provided with filters at each end and wherein the washing is effected by one way passage through the filters

8. Method according to claims 1-7, wherein the container containing the filter with cells of clinical interest therein is sequentially filled and emptied with each of the Pap solutions for staining the cells in a manner such as to permit cytological examination thereof.

9. Method according to claim 4, wherein the menstrual blood is collected by means of a tampon which is introduced into a container containing the fixative solution, the container is shaken or sonicated whereby the cells from the menstrual blood become suspended in the fixative solution and the thus obtained cell suspension and fixative solution is aspirated into the container provided with the filter.

10. Device for Pap analysis, comprising:

a container provided with openings at two ends,

a filter secured in said container, said filter having a pore size sufficiently small to prevent passage through the same of cells of clinical interest for Pap analysis while being sufficiently large to permit cells not of such clinical interest to pass through the same, and

means for passing washing fluid through the filter for washing out cells not of clinical interest, the cells of clinical interest being retained therein because of the pore size of the filter.

11. Device according to claim 10, wherein said container is provided with filters at two ends thereof.

12. Device according to claims 10 or 11 and including means for controlling fluid flow through the filter(s) and means for closing and opening the openings at the ends of the container for the washing of the specimen contained in the same and removal of fluid and cells not of clinical interest through the filter.

FIG. 1

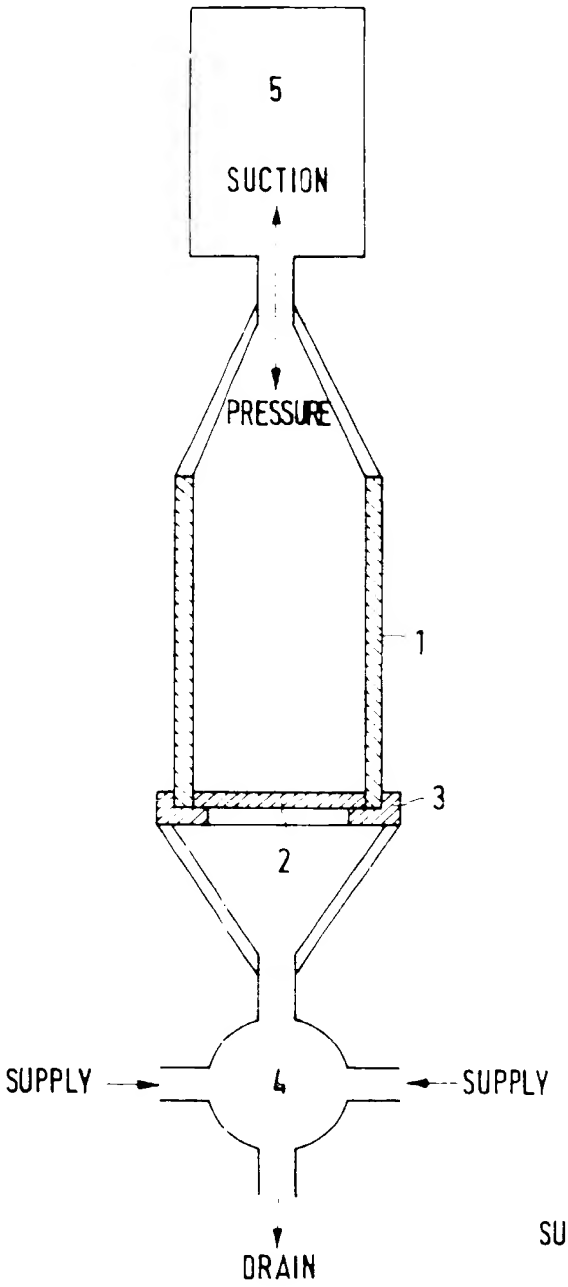


FIG. 2

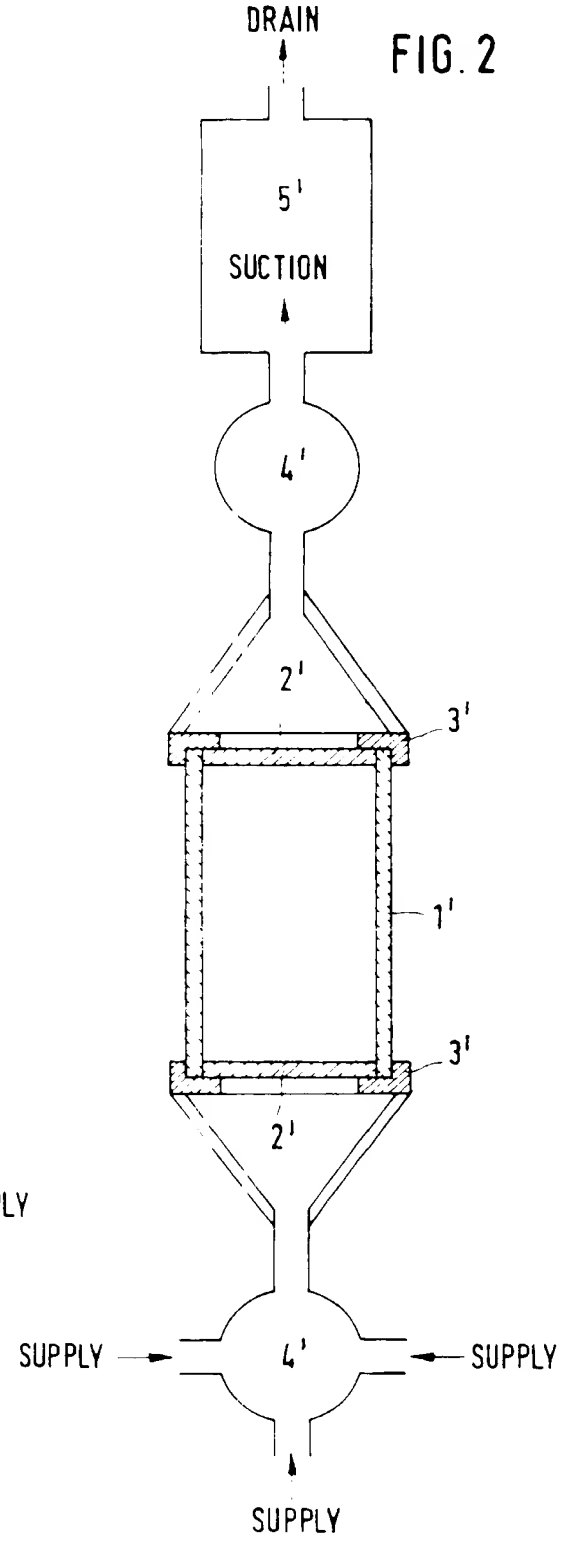


FIG.3

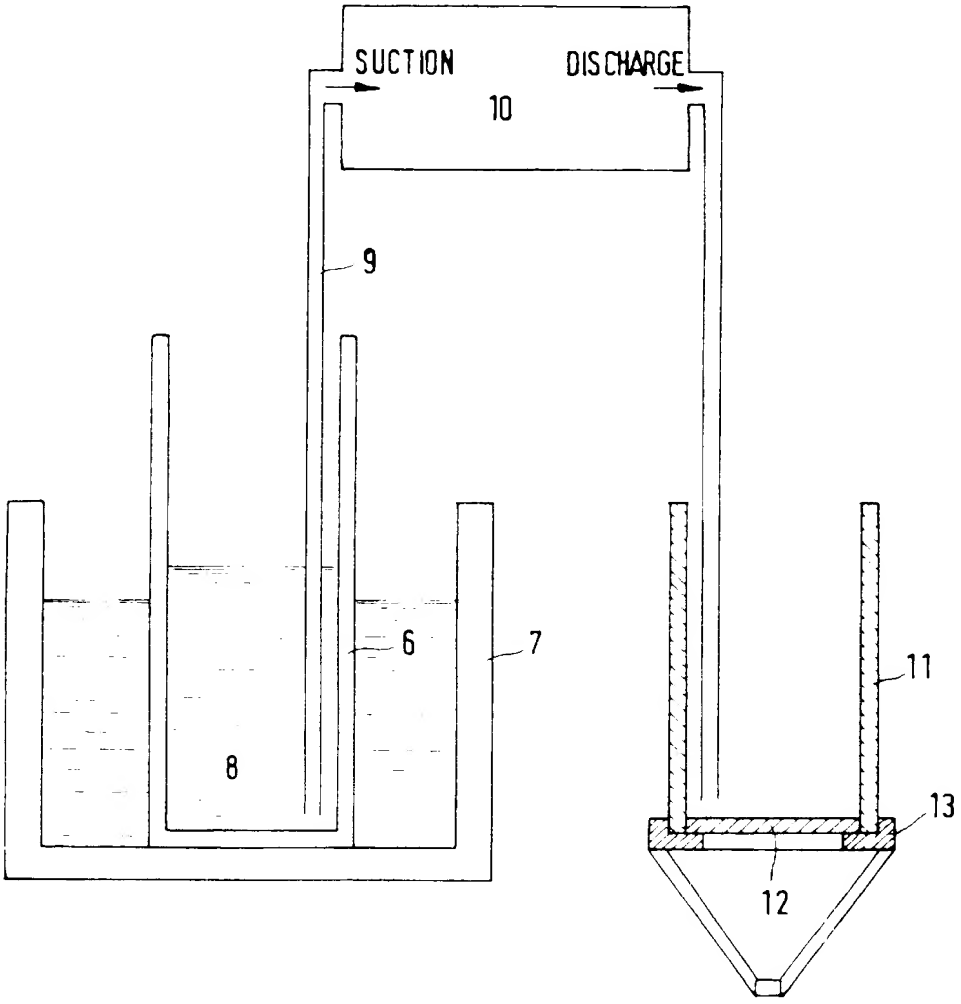
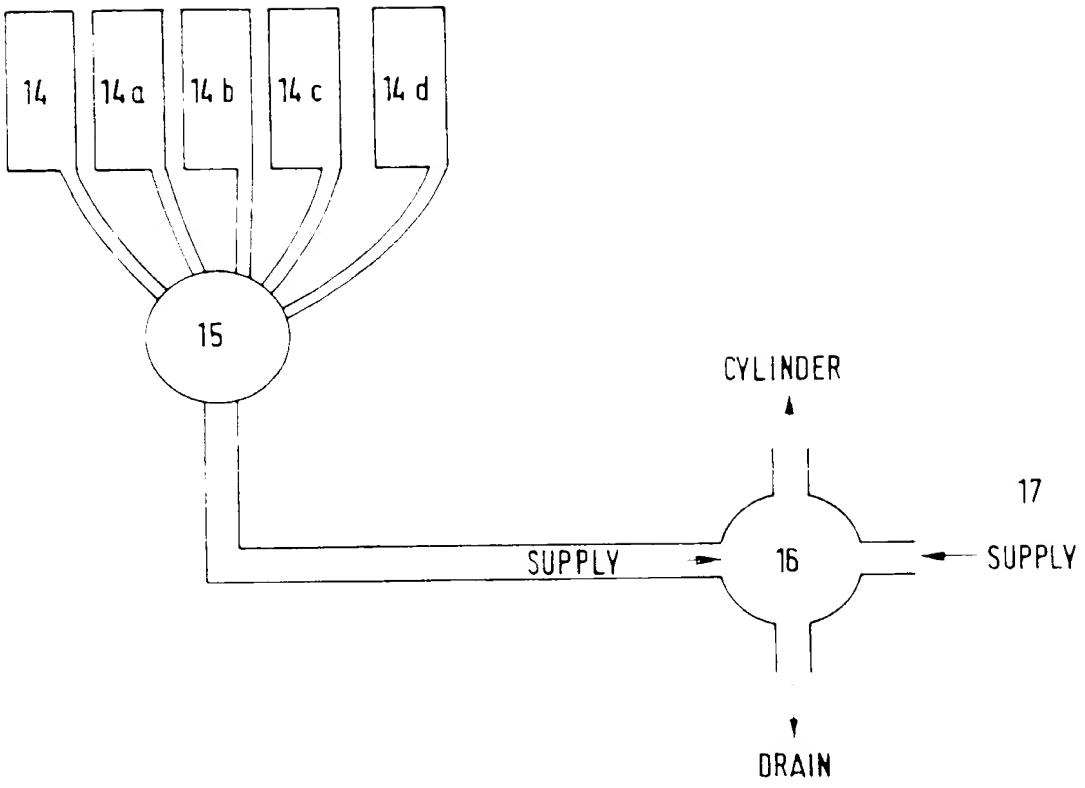


FIG. 4



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EUROPEAN SEARCH REPORT

Application Number

EP 91 11 6260

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	DE-A-2 800 171 (L. BUCALO)	1-6, 8-10,12	C12M1/26 G01N1/30
Y	* claims 1,5,8,10; figures * * page 6, paragraph 1-2 * * page 7, paragraph 4 * * page 9, paragraph 2 - page 10, paragraph 1 * ---	1,7,11	
Y	EP-A-0 088 971 (BOEHRINGER MANNHEIM GMBH) * claims; figures * -----	1,7,11	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

C12M
G01N

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	11 DECEMBER 1991	COUCKE A.O.M.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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